Citation:

Pittas AG, Roberts SB, Das SK, Gilhooly CH, Saltzman E, Golden J, Stark PC, Greenberg AS. The effects of the dietary glycemic load on type 2 diabetes risk factors during weight loss. *Obesity (Silver Spring)*. 2006 Dec; 14(12): 2,200-2,209.

PubMed ID: 17189547

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine whether two calorie-restricted diets that differ in glycemic load have differential effects on major risk factors for development of type 2 diabetes, in particular, glucose-insulin dynamics and plasma C-reactive protein (CRP) concentration.

Inclusion Criteria:

Healthy adults aged 24 to 42 years with a body mass index (BMI) of 25 to 29.9kg/m^2 and a fasting plasma glucose level of less than 100mg per dL.

Exclusion Criteria:

- Subjects with greater than a 15-pound weight change during the previous year
- Known serious medical condition (such as diabetes, cancer, heart disease, endocrine disorder, acquired immunodeficiency syndrome, depression, eating disorder)
- Anemia
- Hypertension
- Abnormal electrocardiogram
- Liver, kidney or thyroid dysfunction
- Strong family history of heart disease, cancer or diabetes
- Pregnancy, lactation or planned to become pregnant in the following year
- Heavy participation in sports activities (more than 12 hours per week)
- Known nutritional and lifestyle issues that could prevent participation in and completion of the study
- Unwilling or unable to complete an accurate food record.

Description of Study Protocol:

Recruitment

Subjects were recruited from the greater Boston metropolitan area.

Design

Randomized six-month two arm parallel trial.

Dietary Intake/Dietary Assessment Methodology

Daily nutrient intake was calculated from subjects' reports of leftover food and extra items; subjects were to report additional food and drinks eaten other than that provided.

Blinding Used

- Subjects were not informed of their randomization for the first 12 weeks of the intervention
- All outcome and data management study personnel were blinded to treatment allocation
- The dietary study intervention personnel were not blinded.

Intervention

After a seven-week baseline period, when usual energy requirements for weight stability were measured, subjects were randomized for 24 weeks to either a high glycemic load diet or a low glycemic load diet. Both diets provided 30%calorie restriction compared with individual baseline weight maintenance energy requirements. Subjects were also provided with a multivitamin supplement and calcium 500mg per day to ensure that Dietary Reference Intakes (DRI) for micronutrients were met. All food was provided during the six months by the research center and collected for home consumption twice weekly by the participants or their designated representative. Subjects were expected to consume only this food; however, they were to report additional foods or drinks if they were eaten. Subjects attended regular behavioral group meetings and individual sessions with a dietitian.

- High-glycemic load diet: 60% carbohydrate, 20% protein, 20% fat, 1kcal per g energy density, fiber 15g per 1,000kcal, with a mean estimated daily glycemic index of 86 and a mean estimated daily glycemic load of 116g per 1,000kcal
- Low-glycemic load diet: 40% carbohydrate, 30% protein, 30% fat, 1kcal per g energy density, fiber 15g per 1,000kcal, with a mean estimated daily glycemic index of 53 and a mean estimated daily glycemic load of 45g per 1,000kcal.

Statistical Analysis

- To examine differences in baseline characteristics between groups, T-tests and chi-square tests were used
- To compare within-group mean changes in outcomes (baseline, three months and six months after the intervention), paired T-tests were used
- To compare between-group differences over time for all outcomes, general linear models adjusting for baseline values and changes in weight were used.

Data Collection Summary:

Timing of Measurements

- Body weight was measured weekly

- Height was measured at baseline
- Metabolic measurements were performed after an overnight 12-hour fast at the end of the baseline period, and at weeks 12 and 24. These measures included insulin sensitivity using the homeostasis model assessment of insulin resistance, oral glucose tolerance test to measure glucose tolerance and insulin sensitivity, and CRP concentration
- A frequently sampled intravenous glucose tolerance test to examine glucose and insulin dynamics was conducted in a sample of subjects at zero and six months.

Dependent Variables

- CRP concentration
- Fasting insulin concentration
- Fasting glucose concentration
- Insulin sensitivity measured with the homeostasis model assessment of insulin resistance
- Incremental areas under the curve for glucose and insulin responses after an oral glucose tolerance test
- Insulin sensitivity index (minimal model analysis using MinMod software), incremental first-phase acute insulin response to glucose (area under the curve, insulin above the baseline in the first ten minutes after glucose infusion), and the disposition index (product of insulin sensitivity index and incremental first-phase acute insulin response to glucose) were measured with a frequently sampled intravenous glucose tolerance test.

Independent Variables

- Low-glycemic load diet
- High-glycemic load diet

Control Variables

Baseline values and change in weight.

Description of Actual Data Sample:

- *Initial N:* 34
- *Attrition (final N):* 32 (16 in each group, with 13 and 12 females in the high-and low-glycemic load arms, respectively)
- *Mean age:* 34.6 years
- *Ethnicity:* 82% and 88% white in the high- and low-glycemic load arms, respectively
- *Anthropometrics:* Mean BMI of 27.5kg/m^2
- *Location:* Boston, MA.

Summary of Results:

Key Findings

- Adjusted for baseline weight, weight loss was equivalent in the two groups (7.2 and 7.7kg in the high- and low-glycemic load groups at six months, respectively; P=0.69)
- Within-group declines in fasting glucose at three and six months were not significant (NS)
- Within-group fasting insulin and insulin sensitivity (HOMA-IR) were lower at six months compared to baseline levels (P<0.05)

- After adjusting for baseline values and changes in weight, there were NS differences between the two groups at three or six months in fasting insulin, glucose or insulin sensitivity (HOMA-IR)
- After adjusting for baseline values and changes in weight, NS differences were observed between the two groups in post-load glucose or insulin values at any individual time-points, or in the area under the curve for either glucose or insulin
- After adjusting for baseline values and change in weight, there were NS differences in measures obtained from the frequently samples intravenous glucose tolerance test between the two groups
- After adjusting for baseline values and change in weight, there were NS difference in the mean CRP change at six months (P=0.13).

Author Conclusion:

Energy-restricted provided diets with high- or low-glycemic load had equivalent weight-loss–adjusted effects on chronic adaptations in glucose-insulin dynamics after six months in overweight individuals with normal fasting plasma glucose. This finding highlights the importance of absolute weight loss, rather than dietary macronutrient composition as the primary determinant of improvements in glucose-insulin dynamics during weight-loss treatment programs.

Reviewer Comments:

- *Author-identified limitations:*
  - *The effect of dietary glycemic load independent of caloric restriction could not be assessed*
  - *The two diets differed in fat and protein content (in addition to carbohydrate quantity and quality)*
  - *Results may not be widely generalizable in individuals with glucose intolerance at baseline or others who are at higher risk of diabetes because of advanced insulin resistance or defective beta cell function at baseline*
- *Author-identified strengths:*
  - *Long study duration*
  - *High retention rate*
  - *Provided foods*
  - *Use of doubly-labeled water method to estimate total energy requirement for calculations of individual energy-restricted prescriptions*
  - *Measurements of glucose tolerance and glucose-insulin dynamics in several ways*
- *Did not identify reasons two participants did not complete the intervention and were not in the analysis.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes

2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A

3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes

6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	???
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	No
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes

9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes